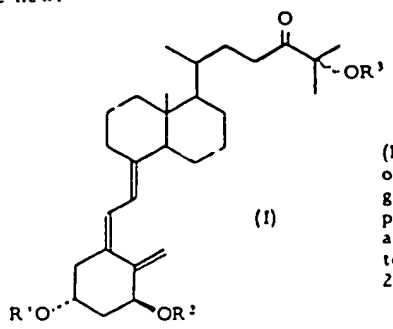


50771 D/28 B05 (B01) TEIJ 26.10.79
 TEIJIN KK *J56061-351
 26.10.79-JP-137771 (26.05.81) A61k-31/59 C07c-172
 1-Alpha, 25-dihydroxy-24-oxo:cholecalciferol derive -
 exhibit vitamin/D 3 pharmacological activities. prepd. from
 24-oxo-cholesta-5,7-diene cpds.

1a, 25-Dihydroxy-24-oxocholecalciferols of formula (I)
 are new:

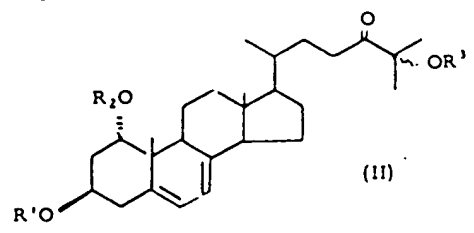


(R¹, R² and R³ = H
 or hydroxy protecting
 gp. (pref. 1-12C ali-
 phatic or aromatic
 acyl, trialkylsilyl, 2-
 tetrahydropyranyl, or
 2-tetrahydrofuranyl)).

B(1-D2, J-G). 2 105

USE/ADVANTAGE
 (I) exhibit vitamin D₃-like pharmacological activities.
 On reduction of the 24-oxo, (I) are converted into 1a, 24,
 25-trihydroxyvitamin D₃ as active vitamin D₃.

PREPARATION
 (I) are prepd. by irradiating 1a,25-dihydroxy-24-oxo-
 cholesta-5,7-dienes (II) with ultraviolet rays to yield 1a,25-
 dihydroxy-24-oxoprevitamins D₃, isomerising the latter
 with thermal energy, if required followed by removal of the
 hydroxy protecting gp.



J56061351+

The UV rays pref. have wavelength 200-360 nm, esp. 260-
 310 nm. The reaction is conducted in an inert solvent-
 including hydrocarbons and halo hydrocarbons (e.g. hexane,
 heptane, PhH, PhMe, xylene, PhCl), ethers (e.g. Et₂O, THF,
 dioxane), and alcohols (e.g. MeOH, EtOH, PrOH) at a temp.
 of -20°C to 120°C, pref. -10°C to 50°C. The subsequent
 thermal isomerisation is carried out at 20-120°C, pref.
 40-100°C in the inert solvent.

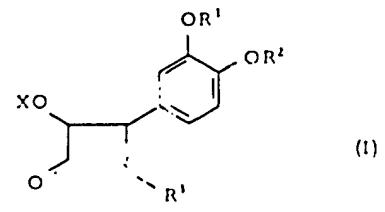
EXAMPLE
 A soln. of 70 mg 1a,3β,25-trihydroxy-24-oxocholesta-5,7-
 diene dissolved in a mixt. of 50 mg deoxygenated EtOH and
 500 ml Et₂O was irradiated with a 200W lamp surrounded by
 a Vycor filter at 10-20°C with stirring for 6 hrs. The
 cold soln. was evapd. in vacuo at 30°C, and the residue was
 dissolved in 250 ml deoxygenated PhH and refluxed under
 heating for 2.5 hr. After the reaction completion, the mixt.
 was evapd. in vacuo, and the resulting residue was chroma-
 tographed on a thin layer of silica gel preliminarily treat-
 ed with 2% AgNO₃-MeCN (solvent:CHCl₃-MeOH) and of sil-
 ica gel (PhH-Me₂CO) to give 10.8 mg 1a,25-dihydroxy-24-
 oxovitamin D₃, mp. 91-93.5°C. (6ppW52)

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50772 D/28 B03 SAGA 24.10.79
 SAGAMI CHEM RES CENTRE *J56061-352
 24.10.79-JP-13485 (26.05.81) C07c-101/77 C07d-205/08
 3-Hydroxy-beta-lactam cpds. can be prepd. economically -
 and are used in DOPA prepn. used in antiparkinson
 treatment.

3-Hydroxy-β-lactam cpds. of formula (I) are new:



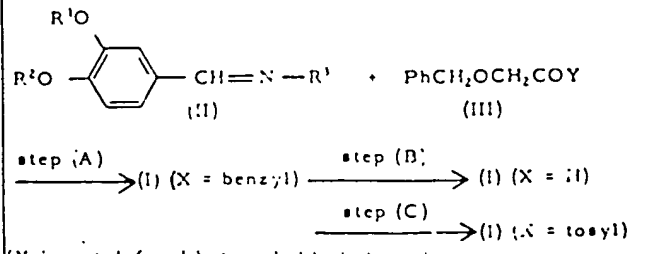
(R¹ and R² = H, lower alkyl, benzyl or acyl, or R¹ and R²
 taken together may form alkylene;
 R¹ = alkyl, aryl or heteroaromatic gp.;
 X = H, benzyl or tosyl).

USE/ADVANTAGE
 (I) can be converted into DOPA (useful as antiparkinson-

B(6-A2, 7-D1). 2 110

isim agent) on reaction with NaN₃, cleavage of the β-lactam
 ring, and acid treatment. (I) can be prepd. from cheap
 raw material.

PREPARATION:



(Y is not defined but probably halogen).
 Step (A) is carried out in a solvent, e.g. PhH, PhMe, THF,
 CH₂Cl₂, in presence of a tert. amine, e.g. Et₃N, Pr₃N,
 Bu₃N, pyridine, N-methylpiperidine, N-methylpyrrolidine
 DBU, at -78°C to 100°C.

J56061352+

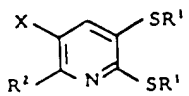
Step (B) comprises hydrogenolysis with Pd catalyst (e.g. Pd black, Pd-C) in a solvent (e.g. MeOH, EtOH, CH₂Cl₂, CHCl₃, PhH, PhMe, THF, MeCN, DMF) at room temp. to 150°C, pref. 50-100°C.
 Step (C) comprises tosylation with p-TsCl in presence of a tert-amine in an aprotic solvent (e.g. CH₂Cl₂, CHCl₃, PhH, PhMe, THF, MeCN, Me₂CO, DMF, DMSO) at -30°C to 100°C.

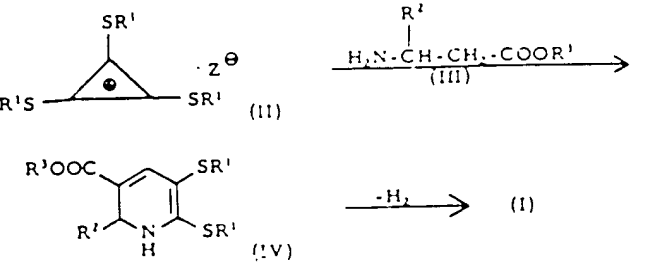
EXAMPLE
 T. a soln. of 5.00 g 3,4-dimethoxybenzylideneaniline and 2.50 g Et₃N in 50 ml PhH was dropwise added slowly a soln. of 4.60 g benzyloxyacetyl chloride in 50 ml PhH under ice cooling. The reaction mixt. was gradually warmed up to room temp., stirred for 15 hrs., washed with water, dried on MgSO₄, and evapd. in vacuo to give 8.18 g light yellow oil. This was chromatographed on silica gel and eluted with n-hexane-EtOAc (4 : 1) to give 4.16 g cis-isomer of 1-phenyl-3-benzyloxy-4-(3,4-dimethoxyphenyl)azetid-2-one as white crystals, m. pt. 130-133°C, and 2.38 g trans-isomer as a colourless oil, n_D²⁰: 1.6018. (IppW52).

J55061352

50774 D/28 B03 C02 E13 MITU 23.10.79
 MITSUBISHI CHEM IND KK *J56061-354
 23.10.79-JP-136740 (26.05.81) C07d-211/90 C07d-213/80
 Nicotinic acid derivs. - used as agrochemicals, drugs and chemical intermediates

BC(7-D4) E(7-D4) N(5-A). 1 1 1 1

Nicotinic acid derivs. of formula (I) are new:
 (I)
 (R¹ = lower alkyl (e.g. Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu);
 R² = H, lower alkyl or aryl (e.g. phenyl, tolyl);
 X = lower alkoxy-carbonyl (e.g. MeOCO-, EtOCO-, n-PrOCO-, i-PrOCO-) or COOH).



(Z⁻ = anion (e.g. halogen ion, ClO₄⁻, BF₄⁻, SbF₆⁻, SbCl₆⁻, AlCl₄⁻);
 R³ = lower alkyl).

DETAILS
 (II) has been described in J48096564.
 The reaction is carried out in a solvent, e.g. CH₂Cl₂, CHCl₃, dimethoxyethane, DMF, MeOH, pref. in presence of a base, e.g. NaH, t-BuOK, at -100°C to the reflux temp. of a base. (J56061354)

USE
 (I) are utilized as agrochemicals or drugs or as raw material in production of various chemicals. (I) can be converted into nicotinic acid or its esters by removal of -SR¹ on hydrogenolysis with Raney Ni catalyst.

PREPARATION

the solvent used, pref. room temp. to 100°C, for a period of 0.1-10 hrs., pref. 0.5-5 hrs.
 The subsequent dehydration is achieved by allowing (IV) to stand in a halogenohydrocarbon solvent, e.g. CHCl₃, CCl₄, fluorohydrocarbon, perfluorohydrocarbon, at 0°C to the reflux temp. of the solvent used, pref. room temp., for a period of 3-24 hrs., pref. 10-15 hrs.

EXAMPLE
 A mixt. of tri-t-butylthiocyclopropenium perchlorate (1 mmole, 403 mg.) and methyl L-aminopropionate (2 mmole) in 40 ml. DMF is allowed to stand at 80°C in presence of NaH (3 mmole) for 1 hr. Water is added, and the mixt. is extracted with hexane. The extract is dried on Na₂SO₄ and evapd., the residue is chromatographed on silica gel to give methyl 2,3-di-t-butylthio-1,6-dihydronicotinate in 72% yield.
 This is dissolved in 10 ml. CCl₄ and allowed to stand under air for 2 hrs. to give methyl 2,3-di-t-butylthio-nicotinate in quantitative yield. (5ppW52)

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